

The specification and claims have been amended to introduce sequence identifiers. No new matter has been added.

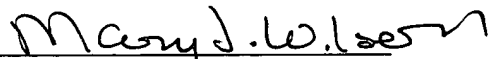
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "Version With Markings To Show Changes Made."

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE, P.C.

By



Mary J. Wilson
Reg. No. 32,955

MJW:tat

1100 North Glebe Road
8th Floor
Arlington, Virginia 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at page 8, line 19:

A preferred nucleotide sequence for a *Rht* gene is one which encodes the RHT amino acid sequence shown in Figure 3b, especially a *Rht* coding sequence shown in Figure 3a. A preferred *rht* mutant lacks part or all of the 17 amino acid sequence underlined in Figure 3b, and/or part or the sequence DVAQKLEQLE (SEQ ID NO:4), which immediately follows the 17 amino acid sequence underlined in Figure 3b.

The paragraph beginning at page 17, line 1:

The present invention also extends to nucleic acid encoding *Rht* or a homologue obtainable using a nucleotide sequence derived from Figure 2 or Figure 3a, and such nucleic acid obtainable using one or more, e.g. a pair, of primers including a sequence shown in Table 1 (SEQ ID NO:21-SEQ ID NO:55).

The paragraph beginning at page 18, line 13:

Some preferred embodiments of polypeptides according to the present invention (encoded by nucleic acid

embodiments according to the present invention) include the 17 amino acid sequence which is underlined in Figure 3b, or a contiguous sequence of amino acids residues with at least about 10 residues with similarity or identity with the respective corresponding residue (in terms of position) in 17 amino acids which are underlined in Figure 3b, more preferably 11, 12, 13, 14, 15, 16 or 17 such residues, and/or the sequence DVAQKLEQLE, or a contiguous sequence of amino acids with at least about 5 residues with similarity or identity with the respective corresponding residue (in terms of position) within DVAQKLEQLE, more preferably 6, 7, 8 or 9 such residues. Further embodiments include the 27 amino acid sequence DELLAALGYKVRASDMADVAQKLEQLE (SEQ ID NO:56), or a contiguous sequence of amino acids residues with at least about 15 residues with similarity or identity with the respective corresponding residue (in terms of position) within this sequence, more preferably 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or 26 such residues.

The paragraph beginning at page 41, line 25:

Figure 1: Alignment of N-terminus predicted GAI amino acid sequence (Gai) (SEQ ID NO:78) with rice EST D39460

(0830) (SEQ ID NO:79), with a region of homology outlined in black.

The paragraph beginning at page 42, line 3:

Figure 2a shows a consensus DNA sequence cDNA C15-1 (obtained via single-pass sequencing) (SEQ ID NO:57).

The paragraph beginning at page 42, line 6:

Figure 2b shows data from original DNA sequencing runs from 14a1 (single-pass) (SEQ ID NO:58-SEQ ID NO:70).

The paragraph beginning at page 42, line 9:

Figure 2c shows data from original DNA sequencing runs from 5a1 (single-pass) (SEQ ID NO:71-SEQ ID NO:77).

The paragraph beginning at page 42, line 14:

Figure 3a shows a composite DNA sequence of wheat *Rht* gene derived from data in Figure 2, including coding sequence (SEQ ID NO:3).

The paragraph beginning at page 42, line 17:

Figure 3b shows an alignment of the entire predicted Rht protein sequence encoded by the coding sequence of Figure 2 (rht) with the entire predicted GAI protein sequence of Arabidopsis (Gai) (SEQ ID NO:1 and SEQ ID NO:2). Regions of sequence identity are highlighted in black.

The paragraph beginning at page 42, line 25:

Figure 4a shows DNA sequence (single-pass) of rice cDNA D39460 (SEQ ID NO:19). This cDNA is an incomplete, partial clone, missing the 3' end of the mRNA from which it is derived.

The paragraph beginning at page 43, line 1:

Figure 4b shows alignment of the entire predicted Rht protein sequence (wheat - encoded by the coding sequence of Figure 2) with that of GAI (Gai) and rice protein sequence predicted from DNA sequence in Figure 4a (Rice) (SEQ ID NO:20). Regions of amino acid identity are highlighted in black; some conservative substitutions are shaded.

The paragraph beginning at page 43, line 12:

Figure 6a shows the nucleotide sequence of rice EST D39460, as determined by the present inventors (SEQ ID NO:12).

The paragraph beginning at page 43, line 15:

Figure 6b shows the predicted amino acid sequence (SEQ ID NO:5) encoded by the rice EST sequence of Figure 6a.

The paragraph beginning at page 43, line 20:

Figure 7a shows the nucleotide sequence of the wheat C15-1 cDNA (SEQ ID NO:13).

The paragraph beginning at page 43, line 23:

Figure 7b shows the predicted amino acid sequence (SEQ ID NO:6) of the wheat C15-1 cDNA of Figure 7a.

The paragraph beginning at page 43, line 28:

Figure 8a shows the nucleotide sequence of the 5a1 wheat genomic clone (SEQ ID NO:14).

The paragraph beginning at page 44, line 3:

Figure 8b shows the predicted amino acid sequence (SEQ ID NO:7) of the 5a1 wheat genomic clone of Figure 8a.

The paragraph beginning at page 44, line 8:

Figure 9a shows the nucleotide sequence of the 1a1 maize genomic clone, i.e. D8 (SEQ ID NO:15).

The paragraph beginning at page 44, line 11:

Figure 9b shows the amino acid sequence (SEQ ID NO:8) of the maize 1a1 genomic clone of Figure 9a.

The paragraph beginning at page 44, line 21:

Figure 11a shows a partial nucleotide sequence of the maize D8-1 allele (SEQ ID NO:16).

The paragraph beginning at page 44, line 24:

Figure 11b shows a partial amino acid sequence (SEQ ID NO:9) of the maize D8-1 allele.

The paragraph beginning at page 44, line 27:

Figure 11c shows a partial nucleotide sequence of the maize D8-2023 allele (SEQ ID NO:17).

The paragraph beginning at page 45, line 1:

Figure 11d shows a partial amino acid sequence (SEQ ID NO:10) of the maize D8-2023 allele.

The paragraph beginning at page 45, line 6:

Figure 12a shows a partial nucleotide sequence of the wheat *rht-10* allele (SEQ ID NO:18).

The paragraph beginning at page 45, line 9:

Figure 12b shows a partial amino acid sequence (SEQ ID NO:11) of the wheat *rht-10* allele.

The paragraph beginning at page 45, line 23:

Previously, we cloned the *GAI* gene of *Arabidopsis* (PCT/GB97/00390 - WO97/29123 published 14 August 1997). Comparison of the DNA sequences of the wild-type (*GAI*) and mutant (*gai*) alleles showed that *gai* encodes a mutant predicted protein product (*gai*) which lacks a segment of 17 amino acids from close to the N-terminus of the protein.

Screening of the DNA sequence databases with the *GAI* sequence revealed the existence of a rice EST (D39460) which contains a region of sequence very closely related to that of the segment that is deleted from *GAI* in the *gai* protein. A comparison of the predicted amino acid sequences from the region DELLA (SEQ ID NO:107) to EQLE (SEQ ID NO:108) are identical in both sequences. The two differences (V/A; E/D) are conservative substitutions, in which one amino acid residue is replaced by another having very similar chemical properties. In addition, the region of identity extends beyond the boundary of the deletion region in the *gai* protein. The sequence DVAQKLEQLE is not affected by the deletion in *gai*, and yet is perfectly conserved between the *GAI* and D39460 sequences (Figure 1).

The paragraph beginning at page 49, line 20:

Mutations were found in the candidate *D8* and *Rht* genes in each of the above mutants. The *D8*-1 mutation is an in-frame deletion which removes amino acids VAQK (SEQ ID NO:101) (55-59) and adds a G (see sequence in Figure 11a and Figure 11b). This deletion overlaps with the conserved DVAQKLEQLE homology block described above. *D8*-2023 is another in-frame deletion mutation that removes amino acids

LATDTVHYNPSD (SEQ ID NO:102) (87-98) from the N-terminus of the D8 protein (see Figure 11c and Figure 11d). This deletion does not overlap with the deletion in gai or D8-1, but covers another region that is highly conserved between GAI, D8 and Rht (see Figure 10). Finally, *Rht-D1c* contains another small in-frame deletion that removes amino acids LNAPPPPLPPAPQ (SEQ ID NO:103) (109-121) in the N-terminal region of the mutant Rht protein that it encodes (see Figure 12a and Figure 12b) (LN-P is conserved [between] between GAI, D8 and Rht, see Figure 10).

The paragraph beginning at page 52, line 1:

TABLE 2 - Primers used in the sequence of D-8 clones (SEQ ID NO:80-SEQ ID NO:100)

IN THE CLAIMS:

1. (Amended) An isolated polynucleotide encoding a polypeptide which comprises the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104) and which on expression in a *Triticum Aestivum* plant provides inhibition of growth of the plant, which inhibition is antagonised by gibberellin.

3. (Amended) An isolated polynucleotide according to claim 2 which includes the nucleotide sequence of nucleic acid obtainable from *Triticum Aestivum* encoding the Rht polypeptide, the nucleotide sequence including GACGAGCTGCTGGCGGCGCTCGGGTACAAGGTGCGCGCCTCCGACATGGCG (SEQ ID NO:105).

4. (Amended) An isolated polynucleotide encoding a polypeptide which comprises the amino acid sequence shown in Figure 8b (SEQ ID NO:7).

5. (Amended) An isolated polynucleotide according to claim 4 which has the coding nucleotide sequence shown in Figure 8a (SEQ ID NO:14).

6. (Amended) An isolated polynucleotide encoding a polypeptide which on expression in a plant provides inhibition of growth of the plant, which inhibition is antagonised by gibberellin, wherein the polypeptide has an amino acid sequence which shows at least 80% similarity with the amino acid sequence of the Rht polypeptide of *Triticum Aestivum* encoded by nucleic acid obtainable from *Triticum Aestivum* which includes the nucleotide sequence

GACGAGCTGCTGGCGGCGCTCGGGTACAAGGTGCGCGCCTCCGACATGGCG (SEQ ID NO:105).

7. (Amended) An isolated polynucleotide according to claim 6 wherein said polypeptide includes the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104).

8. (Amended) An isolated polynucleotide according to claim 6 wherein said polypeptide includes a contiguous sequence of 17 amino acids in which at least 10 residues show amino acid similarity or identity with the residue in the corresponding position in the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104).

9. (Amended) An isolated polynucleotide according to claim 8 wherein said polypeptide includes a contiguous sequence of 17 amino acids in which 16 residues show amino acid identity with the residue in the corresponding position in the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104).

10. (Amended) An isolated polynucleotide according to claim 9 wherein said polypeptide includes the amino acid

sequence shown in Figure 9b (SEQ ID NO:8) for the maize D8 polypeptide.

11. (Amended) An isolated polynucleotide according to claim 10 which has the coding nucleotide sequence shown in Figure 9a (SEQ ID NO:15).

12. (Amended) An isolated polynucleotide according to claim 9 wherein said polypeptide includes the amino acid sequence shown in Figure 6b (SEQ ID NO:5).

13. (Amended) An isolated polynucleotide according to claim 12 which has the coding nucleotide sequence shown in Figure 6a (SEQ ID NO:12).

14. (Amended) An isolated polynucleotide encoding a polypeptide which on expression in a plant confers a phenotype on the plant which is gibberellin-unresponsive dwarfism or which on expression in a *rht* null mutant phenotype plant complements the *rht* null mutant phenotype, such *rht* null mutant phenotype being resistance to the dwarfing effect of paclobutrazol, wherein the polypeptide has an amino acid sequence which shows at least 80% similarity with the amino acid sequence of the *Rht*

polypeptide of *Triticum Aestivum* encoded by nucleic acid obtainable from *Triticum Aestivum* which includes the nucleotide sequence

GACGAGCTGCTGGCGGCGCTCGGGTACAAGGTGCGCGCCTCCGACATGGCG (SEQ ID NO:105).

16. (Amended) An isolated polynucleotide according to claim 15 wherein the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104) is deleted.

17. (Amended) An isolated polynucleotide according to claim 15 wherein the amino acid sequence LNAPPPPLPPAPQ (SEQ ID NO:103) is deleted.

18. (Amended) An isolated polynucleotide according to claim 14 wherein the polypeptide includes the amino acid sequence shown in Figure 9b (SEQ ID NO:8) for the maize D8 polypeptide, with one or more amino acids deleted.

19. (Amended) An isolated polynucleotide according to claim 18 wherein the amino acid sequence DELLAALGYKVRSSDMA (SEQ ID NO:106) is deleted.

20. (Amended) An isolated polynucleotide according to claim 19 which has the coding nucleotide sequence shown in Figure 9a (SEQ ID NO:15), wherein the nucleotides encoding the amino acid sequence DELLAALGYKVRSSDMA (SEQ ID NO:106) are deleted.

21. (Amended) An isolated polynucleotide according to claim 18 wherein the amino acid sequence VAQK (SEQ ID NO:101) is deleted.

22. (Amended) An isolated polynucleotide according to claim 18 wherein the amino acid sequence LATDTVHYNPSD (SEQ ID NO:102) is deleted.

23. (Amended) An isolated polynucleotide according to claim 14 wherein the polypeptide includes the amino acid sequence shown in Figure 6b (SEQ ID NO:5), with one or more amino acids deleted.

24. (Amended) An isolated polynucleotide according to claim 23 wherein the amino acid sequence DELLAALGYKVRSSDMA (SEQ ID NO:106) deleted.

25. (Amended) An isolated polynucleotide according to claim 24 which has the coding nucleotide sequence shown in Figure 6a (SEQ ID NO:12), wherein the nucleotides encoding the amino acid sequence DELLAALGYKVRSSDMA (SEQ ID NO:106) are deleted.

26. (Amended) An isolated polynucleotide encoding a polypeptide which comprises the amino acid sequence shown in Figure 8b (SEQ ID NO:7), with the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104) deleted.

27. (Amended) An isolated polynucleotide according to claim 26 which has the coding nucleotide sequence shown in Figure 8a (SEQ ID NO:14), wherein the nucleotides encoding the amino acid sequence DELLAALGYKVRASDMA (SEQ ID NO:104) are deleted.

50. (Amended) A method according to claim 49 wherein said primers are selected from those shown in Tables 1 (SEQ ID NO:21-SEQ ID NO:55) and 2 (SEQ ID NO:80-SEQ ID NO:100).